

## REMARKS

Favorable reconsideration is respectfully requested.

The claims are 11 to 14 and 16 to 22

New claims 20 to 22 are presented which are supported by the disclosure of page 4, lines 21 to 24 of the present specification.

With regard to the rejection in Official Action paragraph 6, it is now recited that "impure" (R)-2-chloromandelic acid is employed as a starting material to distinguish the reagent from the product of the process.

In Official Action paragraph 7, claims 11-19 were rejected under 35 USC 103(a) as being unpatentable over Effenberger et al. (U.S. 4,859,784), further in view of Collet et al. and further in view of McMasters.

This rejection is respectfully traversed.

Effenberger discloses a process for the production of optically active cyanhydrins, starting with an aldehyde, for example an aromatic aldehyde, via the D-oxynitrilase catalyzed addition of hydrogen cyanide. This reaction is carried out in, for example, aromatic hydrocarbon solvents. The solvent used is saturated with water or with an aqueous buffer solution.

The rejection states that the presaturation with water or an aqueous buffer corresponds to the instant co-solvent. This is not correct since according to the present invention, no water and no aqueous buffer is used for the recrystallization step of the hydroxycarboxylic acid. See especially new claims 20-22 which recite organic co-solvents.

Further, the rejection states that the amount of water in the water-saturated aromatic solvent is considered to fall within the scope of instant claim 19. In reply, since according to the present claims no water is used as co-solvent, this is irrelevant.

The rejection, in addition, states that in Examples 1, 2 and 3 according to Effenberger, the cases of benzaldehyde, o- and m-methoxybenzaldehyde proceed with **diastereomeric excesses** of 99.3, 90 and 98% for the crude cyanhydrins. According to the present invention, however, the **enantiomeric excess** is the relevant value, which is to be increased (in addition to the chemical purity). The diastereomeric excess cannot be compared to the enantiomeric excess.

It is true that Effenberger suggests that the crude nitrile solution can be directly used for the hydrolysis step in order to obtain the corresponding optically active 2-hydroxycarboxylic acid.

But this is not the present invention. The crucial point of the present invention is to increase the chemical purity as well as the optical purity of the acids.

Collet discloses the acidic hydrolysis of racemic halomandelonitriles to the corresponding racemic substituted mandelic acids, which then must be reacted with (-)-ephedrine to form the diastereomeric salts. This salt has to be decomposed with an acid, for instance with HCl, and recrystallized to yield the optically enriched respectively pure acid. No ee-value is disclosed and no chemical purity is cited.

Contrary to Collet according to the present invention, optically active nitriles are first produced by enzyme catalyzed addition of hydrogen cyanide to an aldehyde, then the optically active nitrile is hydrolyzed under acidic conditions to the corresponding hydroxycarboxylic acid, which is recrystallized once in an aromatic hydrocarbon, optionally in the presence of a co-solvents.

Therefore, the two processes are very different.

Further, no art-skilled person could conclude from the Collet reference that recrystallization would have the effect of improving the optical purity as well as the chemical purity of the desired optically active hydroxycarboxylic acids, since there is absolutely no suggestion in the Collet reference that a single recrystallization step as disclosed in the present application could improve the optical purity as well as the chemical one.

Further, there is absolutely no suggestion in the Collet reference that the recrystallization (in order to improve the chemical and the optical purity) could be carried out in the hydrolysis medium as presently claimed (claim 16)

In conclusion, the present process is unobvious in view of Collet, since Collet discloses a very different process and since there is absolutely no suggestion or hint in the Collet reference that the optical and chemical purity of hydroxycarboxylic acids, obtained by acidic hydrolysis of optically active nitriles, which are produced by enzyme catalyzed addition of hydrogen cyanide to

an aldehyde, could be improved by a single recrystallization step using aromatic hydrocarbons, optionally with a co-solvent.

The present process is also not obvious over the combined references (Effenberger and Collet), since firstly, none of these references suggests or discloses that the optical and chemical purity of hydroxycarboxylic acids, obtained by acidic hydrolysis of optically active nitriles, could be improved by a single recrystallization step using aromatic hydrocarbons, optionally with a co-solvent and none of them discloses and suggests that the hydrolysis solution obtained by acidic hydrolysis can be treated directly with aromatic hydrocarbons, optionally with a co-solvent as claimed in claim 16.

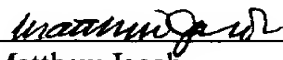
For the foregoing reasons, it is considered that the rejections on prior art are untenable and should be withdrawn.

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact undersigned at the telephone number below.

Respectfully submitted,

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

### IN THE CLAIMS:

*Claim 14 has been amended as follows:*

14. (Amended) The process as claimed in claim 11, wherein impure (R)-2-chloromandelic acid is employed as impure (R)- $\alpha$ -hydroxyacid.